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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,207	11/24/2003	Chang Yi Wang	1151-4153US2	8598

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
05/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,207	WANG ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5-13,16,23 and 24* is/are pending in the application.

4a) Of the above claim(s) *5-13,16,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 3, 5-13,16 and 23-24 are pending.

2. Applicant's election with traverse of Group I, claim 3 and the species of SEQ ID NO:5 in the reply filed on 11/13/2006 is acknowledged. The traversal is on the ground(s) that all of the claims represent a single general inventive concept of an epitope of igE-CH3 domain that is useful when conjugated to promiscuous Th epitopes to generate antibodies against IgE of the treatment of allergies. Applicant contends that although the claims define products with different structures, that their modes of action and physiochemical properties are the same, and that the Examiner has not provided any evidence that they will act any differently. Applicant also argues that the claims have been classified in overlapping class and subclasses. Under Patent law, Applicant argues, it is necessary to present examples of permutation of the claimed IgE-CH3 epitope to obtain proper scope of protection for the invention and to satisfy the enablement requirement under section 112. "If every permutation of a peptide sequence is regarded as a different invention, it would be wrong." applicant states. The burden of the applicant is cited as another reason why the election is improper according to applicant. Finally, applicant argues that amino acids changes do not always define a separate invention like changes between methane and ethane in a chemical compound.

This is not found persuasive because it is well known in the art that a protein's structure determines its function and that homologous peptides often behave differently. Because applicant has described a particular function that is ascribed to more than one peptide does not mean that all functions and modes of action are the same between the two peptides, nor does it mean that the ascribed function is the same between all peptides, absent experimental evidence to confirm a scientist's best guess. For example, a single amino acid single can alter the function of the protein as described in Lazar et al. (PTO-892, Reference V) that teaches in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen.

The classification of the different Groups is only one field of search. Text and structure searches are also necessary in the examination of the inventions of the present application. A search of the structure for claimed immunogens in each of the Groups would not overlap.

Applicant's assertion that patent law requires a presentation of examples of permutations of the claimed IgE-CH3 epitope to obtain proper scope of protection and to satisfy the enablement requirements under section 112 does not apply as an argument against restriction in this case. First, the USPTO does not ever require an applicant to provide permutations of their invention to obtain proper scope. The

maximized scope of a patent issued is only the concern of the applicant and in no way influences the USPTO on a restriction requirement. Second, 112 does not require permutations unless you are trying to support a claimed genus for which you only have support of representative examples. Again, this goes to the maximization of scope of a patent issued and in no way influences the PTO on a restriction requirement.

Further, the burden to an applicant is not a consideration when deciding a restriction requirement. As stated to applicant during the interview on 10/11/2006, if applicant cares to admit on the record that all of the immunogen variants claimed are obvious in view of one another, the restriction requirement may be overcome. However, applicant chose not to admit that they are obvious over one another. Therefore, they must be novel and separate inventions.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 4-13, 15-18 and 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/13/2006.

4. Claim 3 is currently under examination as it reads on a synthetic peptide immunogen of about 50 to about 90 amino acids comprising a helper T cell epitope, SEQ ID NO:5 and optionally SEQ ID NO:13.

5. Paragraph one, line one of the specification should be updated to reflected the status of all related applications including 09/701,623, now U.S. Patent 6,811,782.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "about 50 to about 90 amino acids", "about 25 to about 29 amino acids" and "about 23 amino acid residues." It is unclear how many amino acids constitute "about". One of skill in the art would not know if applicant meant 4 amino acid, as many as 11 amino acids, or even more.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a synthetic peptide of 45 or 63 amino acids consisting of SEQ ID NO:14 or SEQ ID NO:15, which comprises (a) the helper T cell epitope (Th) consisting of SEQ ID NO:9, (b) an IgE-CH3 domain antigen peptide, wherein said IgE -CH3 domain antigen peptide consisting of SEQ ID NO:5; and optionally (c) the immunostimulatory invasin domain consisting of SEQ ID NO:13, does not reasonably provide enablement for a synthetic peptide of **about 50 to about 90 amino acids**, which comprises (a) **a helper T cell epitope** (Th), (b) an IgE-CH3 domain antigen peptide, wherein said IgE -CH3 domain antigen peptide i) is **between about 25 and about 29 amino acids in length** ii) contains two cysteine residues separated by **about 23 amino acid residues**, and iii) is selected from the group consisting of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:84 or **an immunologically functional analog thereof**, wherein **from one to four of the residues in SEQ ID NO:5 is conservatively substituted or deleted**; and optionally (c) an immunostimulatory invasin domain, SEQ ID NO:13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the

invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

In Table 3 of the specification, the results from histamine release inhibition assays using SEQ ID NO:5 and SEQ ID NO:9 with or without SEQ ID NO:13 are shown. SEQ ID NO:14 (SEQ ID NO:5 and SEQ ID NO:9) and SEQ ID NO:15 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13) inhibit 58 and 71% of histamine release.

The specification does not disclose any peptide other than SEQ ID NO:14 (SEQ ID NO:5 and SEQ ID NO:9) and SEQ ID NO:15 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13) comprising SEQ ID NO:5 that can be used in the instant invention.

The specification does not disclose support for the recited "helper T cell epitope (Th)." This recitation includes all helper T cell epitopes, including undiscovered T cell epitopes from undiscovered antigens. The specification's disclosure does not provide

enablement for the use of any helper T cell epitope in the instant invention.

Further, the specification does not disclose support for the 'an immunologically functional analog' of SEQ ID NO:5, 'wherein from one to four of the residues in SEQ ID NO:5 is conservatively substituted or deleted.' The specification's disclosure does not provide enablement for the use of any analog or mutant of SEQ ID NO:5 in the instant invention. The specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 5 is essential for maintain its use in the claimed immunogen for inhibiting histamine release and which changes can be made in the structure of SEQ ID NO: 5 and still maintained the same function. Mutations in the conserved patterns without much change in the overall sequence would lead to a change in the essential structure and therefore to a change in function. Therefore, absent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

The function of a given protein or peptide is unpredictable as demonstrated in the art. For example, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood teaches that "[i]t is presumptuous to make functional assignments merely on

the basis of some degree of similarity between sequences (PTO-892, Reference V). Similarly, Skolnick et al. teaches that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (PTO-892, Reference W, In particular, "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein In particular "Abstract", Box 2). Finally, as supported *supra* even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. shows that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (In particular, Table 2). Thus, it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. The specification has support for using the helper T cell epitope of SEQ ID NO:9 with the IgE-CH3 domain of SEQ ID NO:5, but there is not sufficient support for the recited "helper T cell epitope." Further, the specification does not provide enablement for the use of any analog or mutant of SEQ ID NO:5 in the instant invention.

The recitation of a synthetic peptide of about 50 to about 90 amino acids is not enabled in the claimed invention because the examples in the specification comprising SEQ ID NO:5 lead to a synthetic peptide of 45 or 63 amino acids in length. As written,

the additional unspecified 5 to 27 amino acids included in the synthetic peptide as recited in the claims may be responsible for generating anti-IgE antibodies responsible for inhibiting histamine release and treating allergies and not the peptides of SEQ ID NOs 5, 9 and 13 at all. Given the unpredictability, it would require an undue amount of experimentation by one ordinary skill in the art to practice the invention as claimed.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a synthetic peptide of 45 or 63 amino acids consisting of SEQ ID NO:14 or SEQ ID NO:15, which comprises (a) the helper T cell epitope (Th) consisting of SEQ ID NO:9, (b) an IgE-CH3 domain antigen peptide, wherein said IgE -CH3 domain antigen peptide consisting of SEQ ID NO:5; and optionally (c) the immunostimulatory invasin domain consisting of SEQ ID NO:13.

Applicant is not in possession of: a synthetic peptide of **about 50 to about 90 amino acids**, which comprises (a) **a helper T cell epitope** (Th), (b) an IgE-CH3 domain antigen peptide, wherein said IgE -CH3 domain antigen peptide i) is **between about 25 and about 29 amino acids in length** ii) contains two cysteine residues separated by **about 23 amino acid residues**, and iii) is selected from the group consisting of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:84 or **an immunologically functional analog thereof**, wherein **from one to four of the residues in SEQ ID NO:5 is conservatively substituted or deleted**; and optionally (c) an immunostimulatory invasin domain, SEQ ID NO:13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

Applicant has disclosed and reduced to practice no other than synthetic peptide comprising SEQ ID NO:5 than SEQ ID NO:14 (SEQ ID NO:5 and SEQ ID NO:9) and SEQ ID NO:15 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The specification does not describe any "helper T cell epitope (Th)" for use in the instant invention. Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (Th epitope) to describe the claimed genus, nor does it provide a description of

structural features that are common to species (Th epitopes of SEQ ID NOs:9-12). In essence, the specification simply directs those skilled in the art to go figure out for themselves what **helper T cell epitope** would work. The specification's disclosure is inadequate to describe the claimed genus of a synthetic peptide which comprises any helper T cell epitope.

The specification also does not describe 'an immunologically functional analog' of SEQ ID NO:5, 'wherein from one to four of the residues in SEQ ID NO:5 is conservatively substituted or deleted.' Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the immunologically functional analogs. That is, the specification provides neither a representative number of species to describe the claimed genus, nor does it provide a description of structural features that are common to species. It is unclear what, if any, residues of SEQ ID NO: 5 are essential to maintain its use in the claimed immunogen for inhibiting histamine release and which changes can be made in the structure of SEQ ID NO: 5 which still maintain the same function. The specification directs those skilled in the art to go figure out for themselves what mutants and analogs would work. The specification's disclosure is inadequate to describe the claimed genus of a synthetic peptide which comprises any immunologically functional analog wherein from one to four of the residues in SEQ ID NO:5 is conservatively substituted or deleted.

Further, there is inadequate description in the specification to support the recitation of a synthetic peptide of about 50 to about 90 amino acids because the species disclosed in the specification comprising SEQ ID NO:5 lead to a synthetic peptide of 45 or 63 amino acids in length.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 9, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

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Maher M. Haddad

MAHER M. HADDAD
PRIMARY EXAMINER